

2459-1-003 CIP

Structure-based sequence homology alignment of bromodomains

ZA Loop

	720	740	760	780	800	820
	α_A	α_B	α_C	α_D	α_E	α_F
hsp/cap	719- SKPRDPIQLYSTLSLQVKSIG	719- SKPRDPIQLYSTLSLQVKSIG	719- SKPRDPIQLYSTLSLQVKSIG	719- SKPRDPIQLYSTLSLQVKSIG	719- SKPRDPIQLYSTLSLQVKSIG	719- SKPRDPIQLYSTLSLQVKSIG
hscG5	363- GKELKDPDQVLTUUKLQIKSH	363- GKELKDPDQVLTUUKLQIKSH	363- GKELKDPDQVLTUUKLQIKSH	363- GKELKDPDQVLTUUKLQIKSH	363- GKELKDPDQVLTUUKLQIKSH	363- GKELKDPDQVLTUUKLQIKSH
tcp55	280- LAKSKERSFNQCANVEMKHHQ	280- LAKSKERSFNQCANVEMKHHQ	280- LAKSKERSFNQCANVEMKHHQ	280- LAKSKERSFNQCANVEMKHHQ	280- LAKSKERSFNQCANVEMKHHQ	280- LAKSKERSFNQCANVEMKHHQ
sgcG5	324- AORPKRHDAIQAIGLTELQNA	324- AORPKRHDAIQAIGLTELQNA	324- AORPKRHDAIQAIGLTELQNA	324- AORPKRHDAIQAIGLTELQNA	324- AORPKRHDAIQAIGLTELQNA	324- AORPKRHDAIQAIGLTELQNA
hsp300	1046- KKIEKPELROALMPTLEALYRD	1046- KKIEKPELROALMPTLEALYRD	1046- KKIEKPELROALMPTLEALYRD	1046- KKIEKPELROALMPTLEALYRD	1046- KKIEKPELROALMPTLEALYRD	1046- KKIEKPELROALMPTLEALYRD
hscBP	1083- KKIEKPELROALMPTLEALYRD	1083- KKIEKPELROALMPTLEALYRD	1083- KKIEKPELROALMPTLEALYRD	1083- KKIEKPELROALMPTLEALYRD	1083- KKIEKPELROALMPTLEALYRD	1083- KKIEKPELROALMPTLEALYRD
ceyN1	861- DTVFSQEDLINFLLPVEKLDKSR	861- DTVFSQEDLINFLLPVEKLDKSR	861- DTVFSQEDLINFLLPVEKLDKSR	861- DTVFSQEDLINFLLPVEKLDKSR	861- DTVFSQEDLINFLLPVEKLDKSR	861- DTVFSQEDLINFLLPVEKLDKSR
hscG1-1	1376- RRTDPMVTLSSIESINNRDL	1376- RRTDPMVTLSSIESINNRDL	1376- RRTDPMVTLSSIESINNRDL	1376- RRTDPMVTLSSIESINNRDL	1376- RRTDPMVTLSSIESINNRDL	1376- RRTDPMVTLSSIESINNRDL
hscG1-1	1371- RRTDPMVTLSSIESINNRDL	1371- RRTDPMVTLSSIESINNRDL	1371- RRTDPMVTLSSIESINNRDL	1371- RRTDPMVTLSSIESINNRDL	1371- RRTDPMVTLSSIESINNRDL	1371- RRTDPMVTLSSIESINNRDL
hscG1-2	1498- LUDDDQVAFSPILNIVTQMAV	1498- LUDDDQVAFSPILNIVTQMAV	1498- LUDDDQVAFSPILNIVTQMAV	1498- LUDDDQVAFSPILNIVTQMAV	1498- LUDDDQVAFSPILNIVTQMAV	1498- LUDDDQVAFSPILNIVTQMAV
hscG1-2	1493- LUDDDQVAFSPILNIVTQMAV	1493- LUDDDQVAFSPILNIVTQMAV	1493- LUDDDQVAFSPILNIVTQMAV	1493- LUDDDQVAFSPILNIVTQMAV	1493- LUDDDQVAFSPILNIVTQMAV	1493- LUDDDQVAFSPILNIVTQMAV
hscG1-1	24- KGRVTNQLQYLRVHVALKHHQ	24- KGRVTNQLQYLRVHVALKHHQ	24- KGRVTNQLQYLRVHVALKHHQ	24- KGRVTNQLQYLRVHVALKHHQ	24- KGRVTNQLQYLRVHVALKHHQ	24- KGRVTNQLQYLRVHVALKHHQ
hscG1-1	31- KGRVTNQLQYLRVHVALKHHQ	31- KGRVTNQLQYLRVHVALKHHQ	31- KGRVTNQLQYLRVHVALKHHQ	31- KGRVTNQLQYLRVHVALKHHQ	31- KGRVTNQLQYLRVHVALKHHQ	31- KGRVTNQLQYLRVHVALKHHQ
hscG1-1	31- KGRVTNQLQYLRVHVALKHHQ	31- KGRVTNQLQYLRVHVALKHHQ	31- KGRVTNQLQYLRVHVALKHHQ	31- KGRVTNQLQYLRVHVALKHHQ	31- KGRVTNQLQYLRVHVALKHHQ	31- KGRVTNQLQYLRVHVALKHHQ
hscG1-1	148- NP1PKHCKHALLAKAVARK	148- NP1PKHCKHALLAKAVARK	148- NP1PKHCKHALLAKAVARK	148- NP1PKHCKHALLAKAVARK	148- NP1PKHCKHALLAKAVARK	148- NP1PKHCKHALLAKAVARK
hscG1-2	295- KKGKLSKHLKCHGILKELSKH	295- KKGKLSKHLKCHGILKELSKH	295- KKGKLSKHLKCHGILKELSKH	295- KKGKLSKHLKCHGILKELSKH	295- KKGKLSKHLKCHGILKELSKH	295- KKGKLSKHLKCHGILKELSKH
hscG1-2	304- KKGKLSKHLKCHGILKELSKH	304- KKGKLSKHLKCHGILKELSKH	304- KKGKLSKHLKCHGILKELSKH	304- KKGKLSKHLKCHGILKELSKH	304- KKGKLSKHLKCHGILKELSKH	304- KKGKLSKHLKCHGILKELSKH
hscG1-2	473- KKGKLSKHLKCHGILKELSKH	473- KKGKLSKHLKCHGILKELSKH	473- KKGKLSKHLKCHGILKELSKH	473- KKGKLSKHLKCHGILKELSKH	473- KKGKLSKHLKCHGILKELSKH	473- KKGKLSKHLKCHGILKELSKH
hscG1-2	311- KKGKLSKHLKCHGILKELSKH	311- KKGKLSKHLKCHGILKELSKH	311- KKGKLSKHLKCHGILKELSKH	311- KKGKLSKHLKCHGILKELSKH	311- KKGKLSKHLKCHGILKELSKH	311- KKGKLSKHLKCHGILKELSKH
hscG1-2	626- MEMQUTPLILLRKTLEOLKDTG	626- MEMQUTPLILLRKTLEOLKDTG	626- MEMQUTPLILLRKTLEOLKDTG	626- MEMQUTPLILLRKTLEOLKDTG	626- MEMQUTPLILLRKTLEOLKDTG	626- MEMQUTPLILLRKTLEOLKDTG
hscG1-2	594- SEQFAIQAQIKKMAIMLVRAAN	594- SEQFAIQAQIKKMAIMLVRAAN	594- SEQFAIQAQIKKMAIMLVRAAN	594- SEQFAIQAQIKKMAIMLVRAAN	594- SEQFAIQAQIKKMAIMLVRAAN	594- SEQFAIQAQIKKMAIMLVRAAN
hscG1-2	41- NPTVDVDFVACHLNTIRYKQDQ	41- NPTVDVDFVACHLNTIRYKQDQ	41- NPTVDVDFVACHLNTIRYKQDQ	41- NPTVDVDFVACHLNTIRYKQDQ	41- NPTVDVDFVACHLNTIRYKQDQ	41- NPTVDVDFVACHLNTIRYKQDQ
hscG1-2	174- SSICYLKSLLEQLLEAVATN	174- SSICYLKSLLEQLLEAVATN	174- SSICYLKSLLEQLLEAVATN	174- SSICYLKSLLEQLLEAVATN	174- SSICYLKSLLEQLLEAVATN	174- SSICYLKSLLEQLLEAVATN
hscG1-2	374- TSNHUSPLVQYVUTASCHNOG	374- TSNHUSPLVQYVUTASCHNOG	374- TSNHUSPLVQYVUTASCHNOG	374- TSNHUSPLVQYVUTASCHNOG	374- TSNHUSPLVQYVUTASCHNOG	374- TSNHUSPLVQYVUTASCHNOG
hscG1-2	511- CHRMHKKHKKLYNAVLEARESGT	511- CHRMHKKHKKLYNAVLEARESGT	511- CHRMHKKHKKLYNAVLEARESGT	511- CHRMHKKHKKLYNAVLEARESGT	511- CHRMHKKHKKLYNAVLEARESGT	511- CHRMHKKHKKLYNAVLEARESGT
hscG1-2	647- KSKYMTTMOOKLYNAVLEARESGT	647- KSKYMTTMOOKLYNAVLEARESGT	647- KSKYMTTMOOKLYNAVLEARESGT	647- KSKYMTTMOOKLYNAVLEARESGT	647- KSKYMTTMOOKLYNAVLEARESGT	647- KSKYMTTMOOKLYNAVLEARESGT
hscG1-2	5- HNAPEKTKFDEVLALVGLKNE	5- HNAPEKTKFDEVLALVGLKNE	5- HNAPEKTKFDEVLALVGLKNE	5- HNAPEKTKFDEVLALVGLKNE	5- HNAPEKTKFDEVLALVGLKNE	5- HNAPEKTKFDEVLALVGLKNE
hscG1-2	138- GTNEIDVHKVITQILDALEKQDQ	138- GTNEIDVHKVITQILDALEKQDQ	138- GTNEIDVHKVITQILDALEKQDQ	138- GTNEIDVHKVITQILDALEKQDQ	138- GTNEIDVHKVITQILDALEKQDQ	138- GTNEIDVHKVITQILDALEKQDQ
hscG1-2	1377- SPNPPLKTKKMAIDVINKTQSS	1377- SPNPPLKTKKMAIDVINKTQSS	1377- SPNPPLKTKKMAIDVINKTQSS	1377- SPNPPLKTKKMAIDVINKTQSS	1377- SPNPPLKTKKMAIDVINKTQSS	1377- SPNPPLKTKKMAIDVINKTQSS
hscG1-2	1418- SPNPPLKTKKMAIDVINKTQSS	1418- SPNPPLKTKKMAIDVINKTQSS	1418- SPNPPLKTKKMAIDVINKTQSS	1418- SPNPPLKTKKMAIDVINKTQSS	1418- SPNPPLKTKKMAIDVINKTQSS	1418- SPNPPLKTKKMAIDVINKTQSS
hscG1-2	1373- SPNPPLKTKKMAIDVINKTQSS	1373- SPNPPLKTKKMAIDVINKTQSS	1373- SPNPPLKTKKMAIDVINKTQSS	1373- SPNPPLKTKKMAIDVINKTQSS	1373- SPNPPLKTKKMAIDVINKTQSS	1373- SPNPPLKTKKMAIDVINKTQSS
hscG1-2	1436- SPNPPLKTKKMAIDVINKTQSS	1436- SPNPPLKTKKMAIDVINKTQSS	1436- SPNPPLKTKKMAIDVINKTQSS	1436- SPNPPLKTKKMAIDVINKTQSS	1436- SPNPPLKTKKMAIDVINKTQSS	1436- SPNPPLKTKKMAIDVINKTQSS
hscG1-2	694- AKISPAKCKCKVLLAFCH	694- AKISPAKCKCKVLLAFCH	694- AKISPAKCKCKVLLAFCH	694- AKISPAKCKCKVLLAFCH	694- AKISPAKCKCKVLLAFCH	694- AKISPAKCKCKVLLAFCH
hscG1-2	694- AKISPAKCKCKVLLAFCH	694- AKISPAKCKCKVLLAFCH	694- AKISPAKCKCKVLLAFCH	694- AKISPAKCKCKVLLAFCH	694- AKISPAKCKCKVLLAFCH	694- AKISPAKCKCKVLLAFCH
hscG1-2	865- TKITPDKCKCKVLLAFCH	865- TKITPDKCKCKVLLAFCH	865- TKITPDKCKCKVLLAFCH	865- TKITPDKCKCKVLLAFCH	865- TKITPDKCKCKVLLAFCH	865- TKITPDKCKCKVLLAFCH

Figure 1





09794553-041102

2459-1-003 CIP

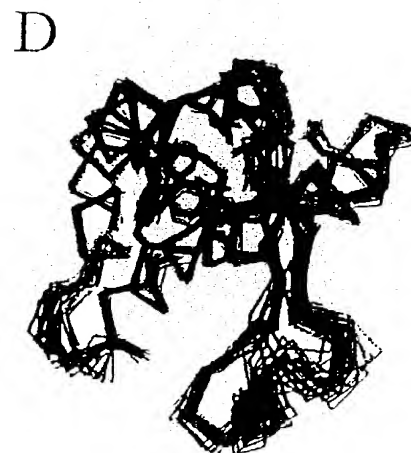
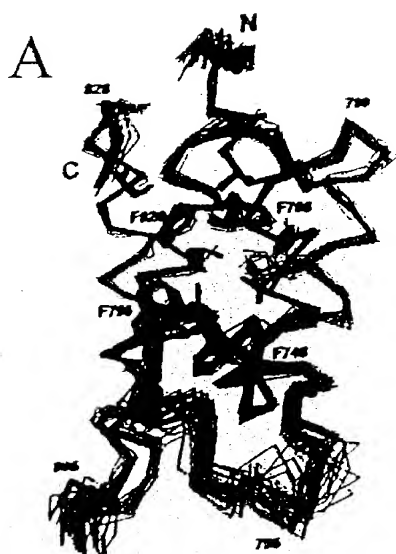


Figure 2A-2D



09784552 041103

2459-1-003 CIP

Three-Dimensional Structure of the P/CAF Bromodomain

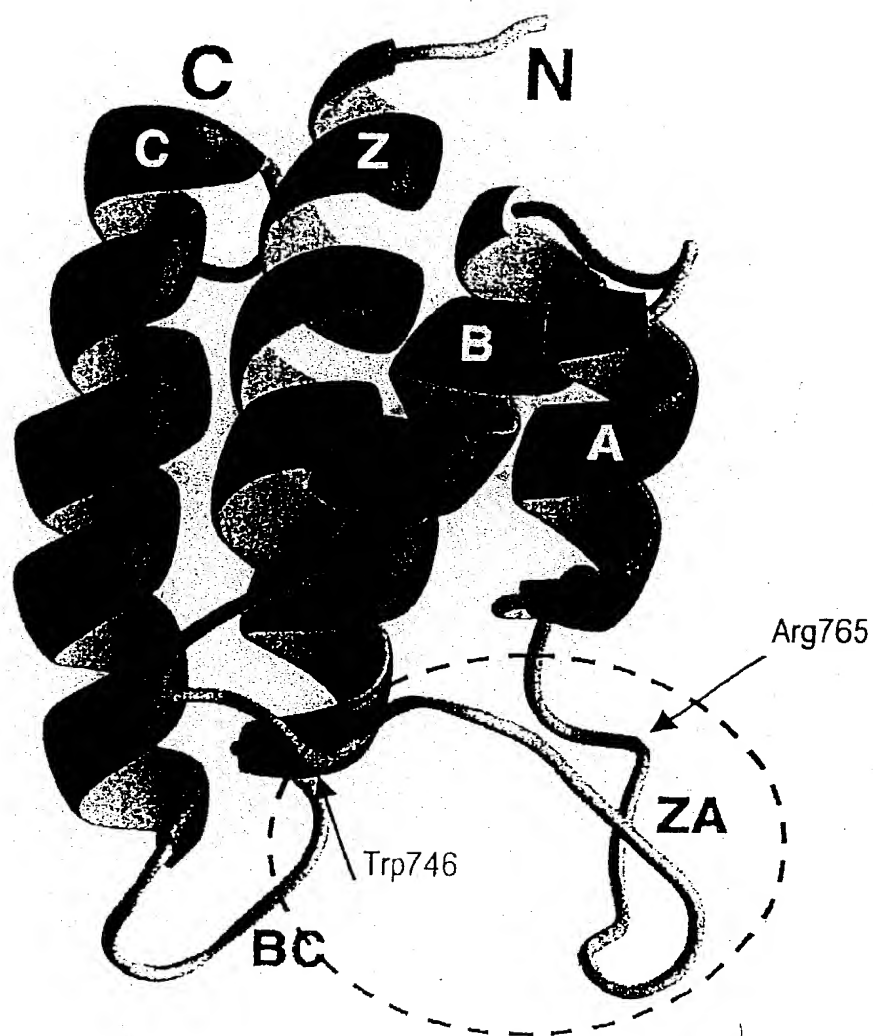


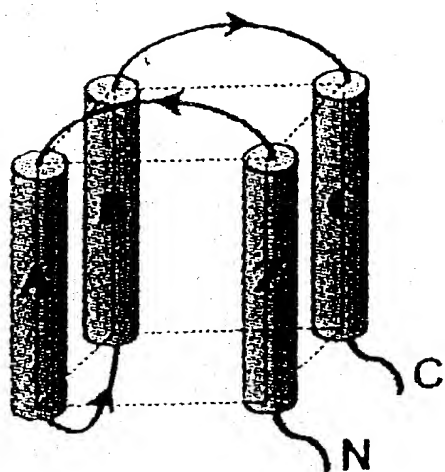
Figure 2E



00724553-041103

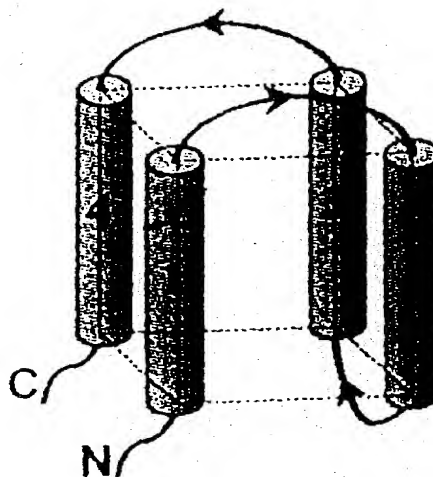
2459-1-003 CIP

F



Left-handed bundle

G



Right-handed bundle

Figure 2F-2G



2459-1-003 CIP

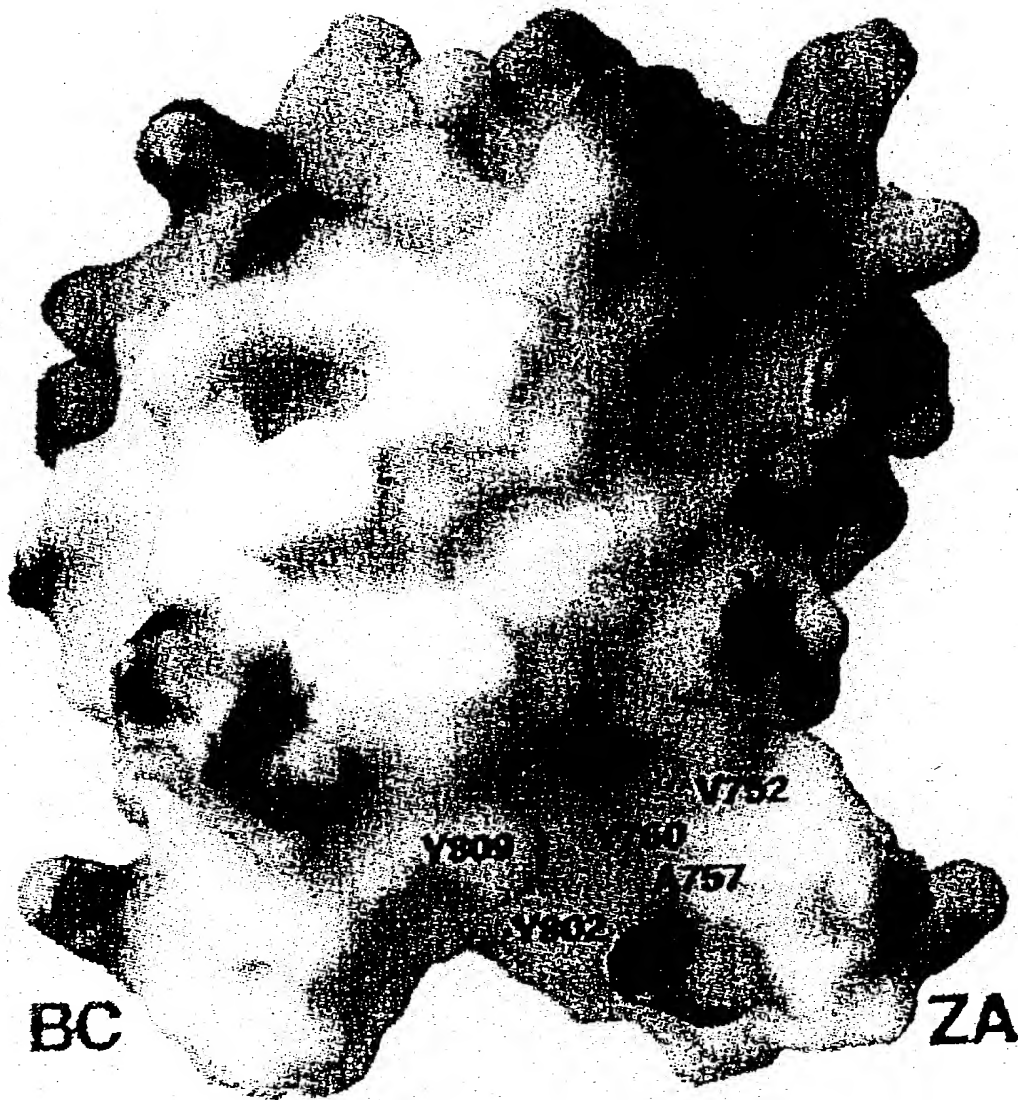


Figure 2H



2459-1-003 CIP

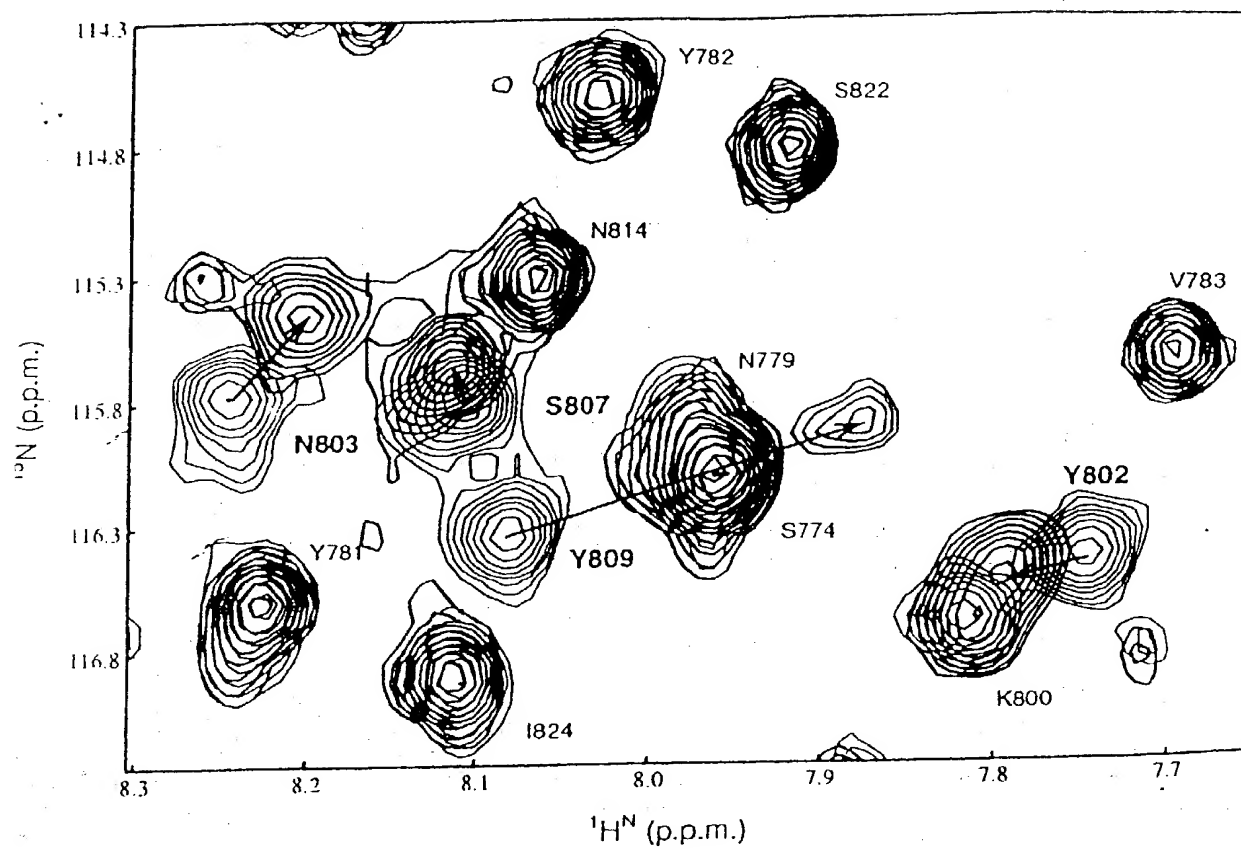


Figure 3A



2459-1-003 CIP

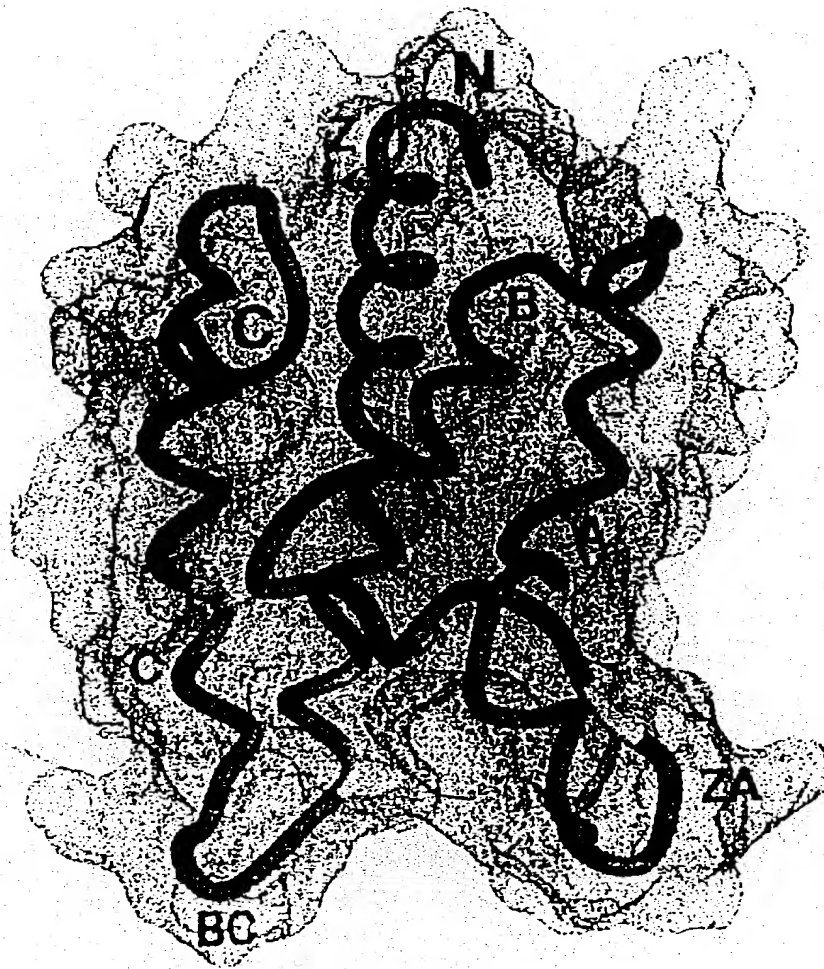
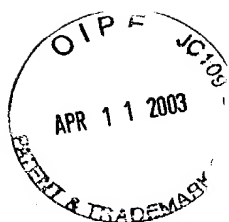
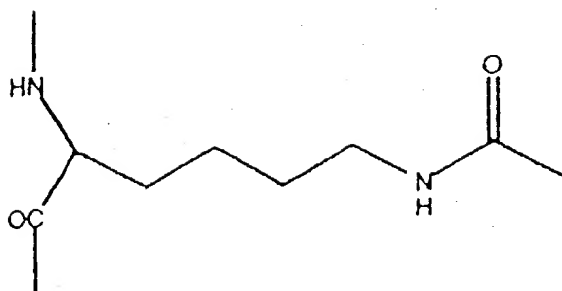


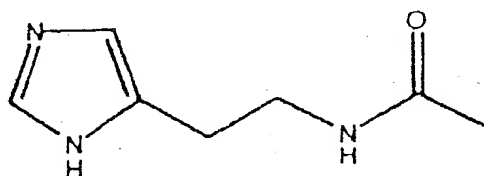
Figure 3B



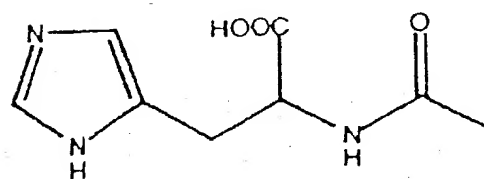
2459-1-003 CIP



N_{ϵ} -acetyl-lysine



N_{ω} -acetyl-histamine



N_{α} -acetyl-histidine

Figure 3C



00794553-041103

2459-1-003 CIP

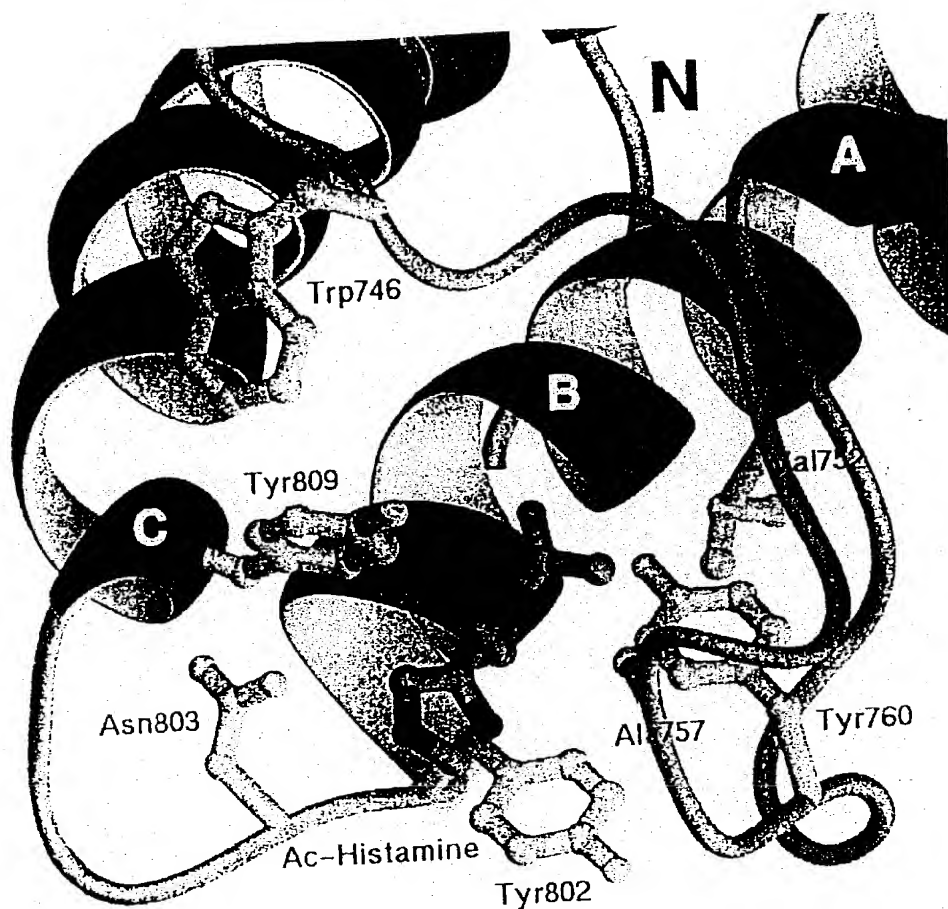
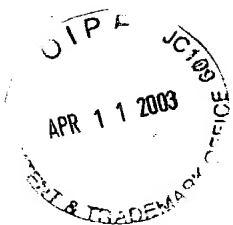


Figure 4



2459-1-003 CIP

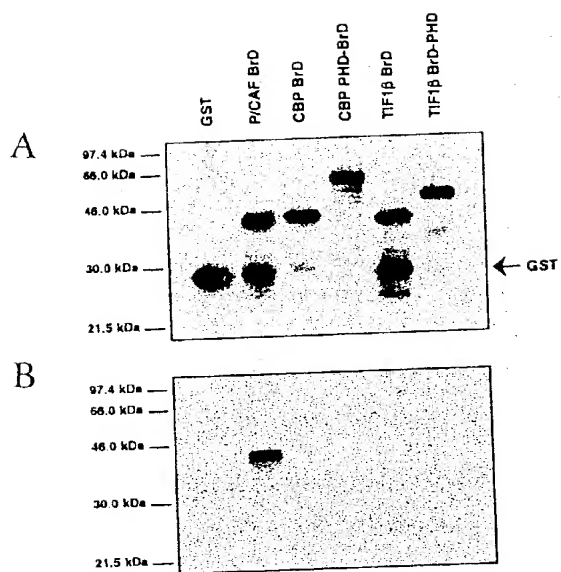


Figure 5



00724552 04-1-02

2459-1-003 CIP

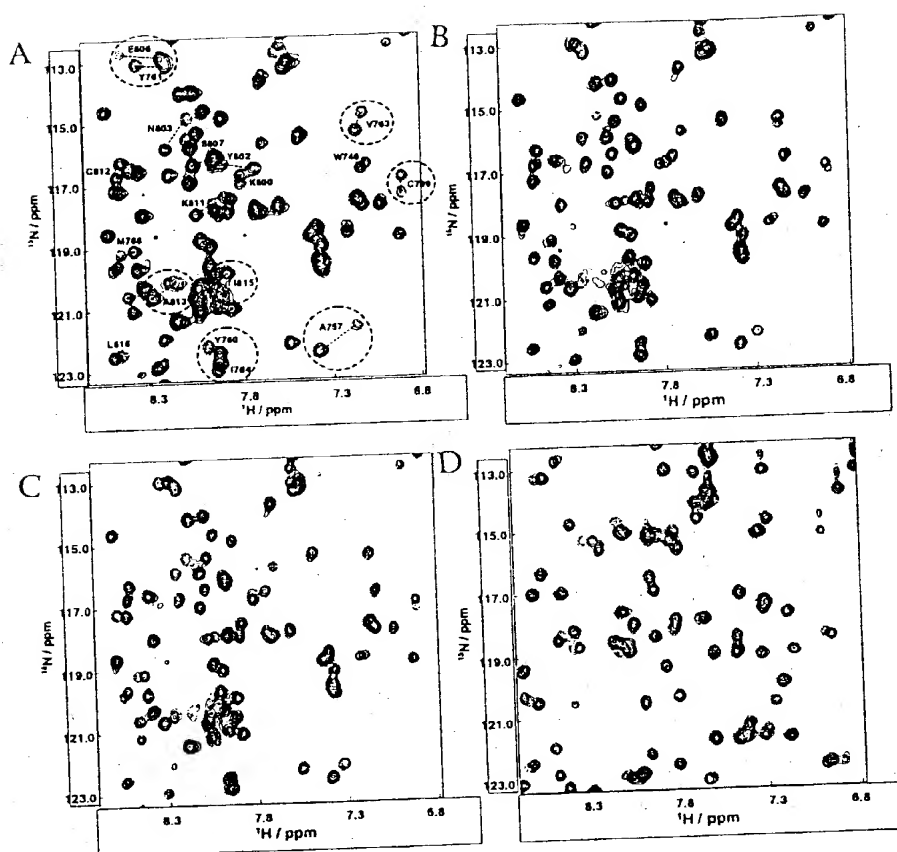


Figure 6



2459-1-003 CIP

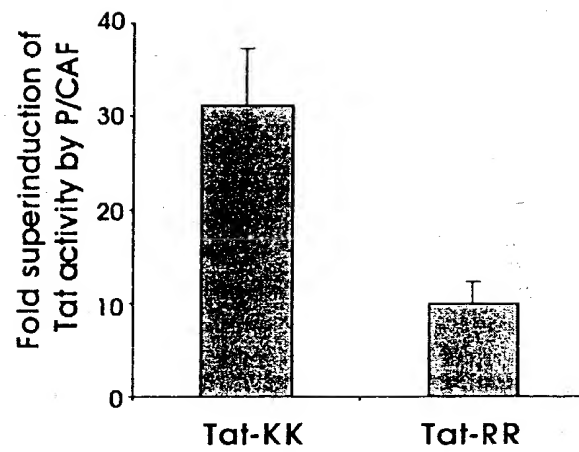
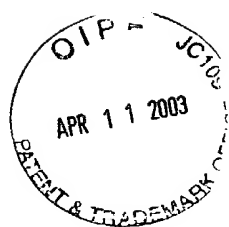


Figure 7



00704552 041103

2459-1-003 CIP

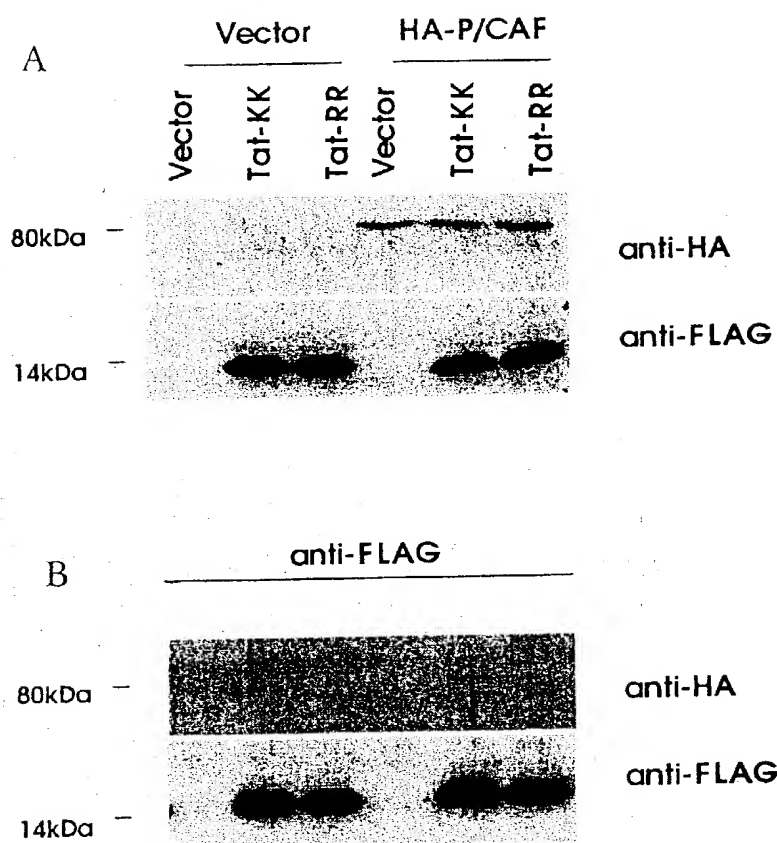
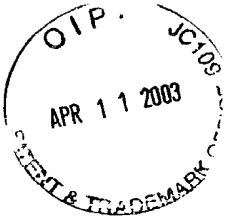
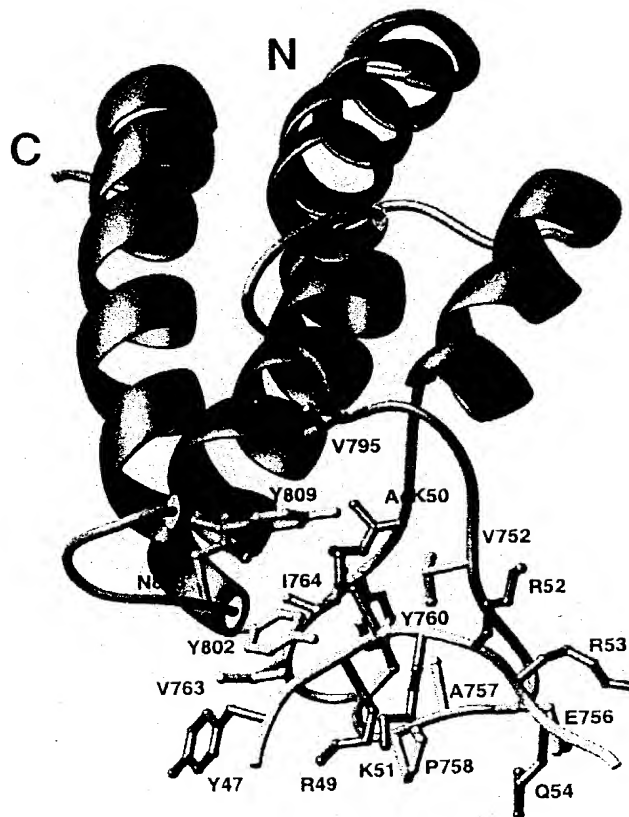


Figure 8



2459-1-003 CIP



HIV-1 Tat Peptide: SYGR-AcK-KRRQRC

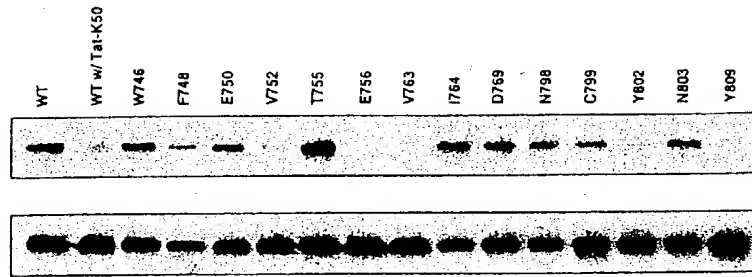
Figure 9



2459-1-003 CIP

2459-1-003 CIP

A



B

- | | |
|--------------------------|-------------------------|
| 1. Control | |
| 2. Tat_K50 (aa 46-55) | SYGR-K-KRRQRC |
| 3. Tat_AcK50 | SYGR-AcK-KRRQRC |
| 4. Tat_AcK50_Y47A | SAGR-AcK-KRRQRC |
| 5. Tat_AcK50_R49A | SYGA-AcK-KRRQRC |
| 6. Tat_AcK50_K51A | SYGR-AcK-ARRQRC |
| 7. Tat_AcK50_R52A | SYGR-AcK-KARQRC |
| 8. Tat_AcK50_R53A | SYGR-AcK-KRAQRC |
| 9. Tat_AcK50_Q54A | SYGR-AcK-KRRARC |
| 10. Tat_AcK51 | SYGRK-AcK-RRQRC |
| 11. Tat_AcK28 (aa 23-33) | TNCYCK-AcK-CCFH |
| 12. Histone H4_AcK16 | SGRGKGGKGLGKGA-AcK-RHRK |

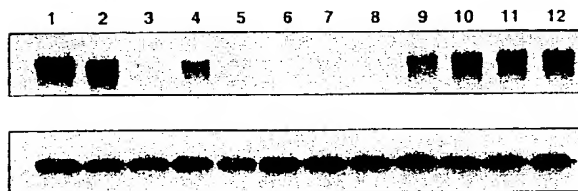


Figure 10



2459-1-003 CIP

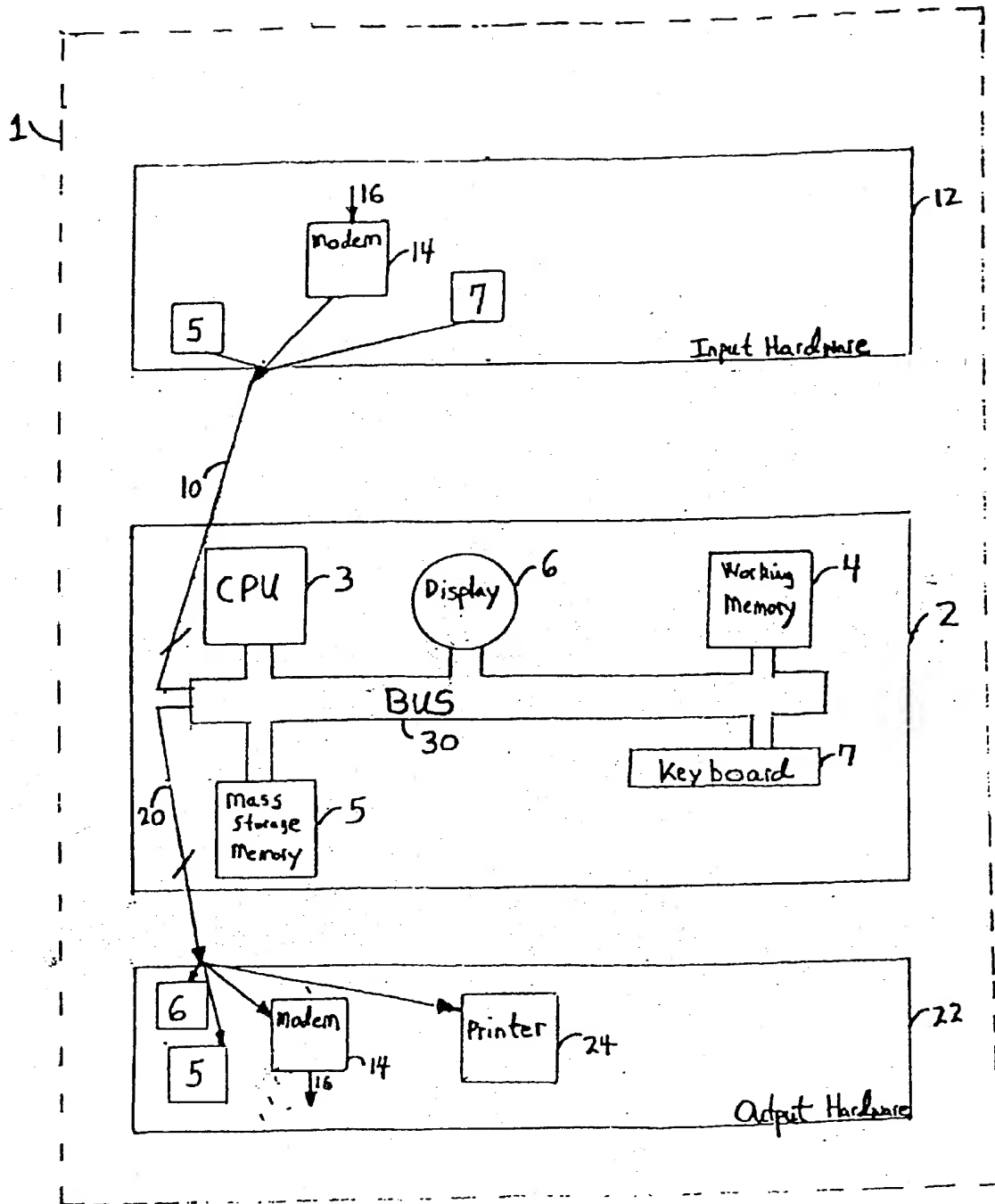
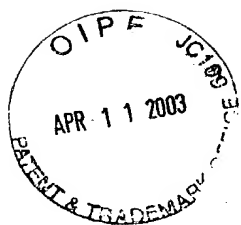
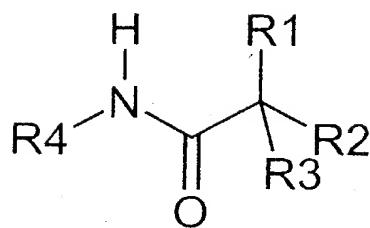


Figure 11



2459-1-003 CIP



Where:

R₁, R₂, R₃ = H, CH₃, X (halogen: F, Cl, Br, I), OH, SH, or NH₃⁺

R₄ = alkyl, aryl

Figure 12